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PREVENTION AND TREATMENT OF
MALARIA

W.E. Deeks

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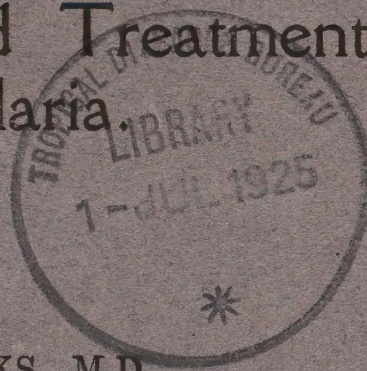
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Prevention and Treatment of Malaria.

BY

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General Manager, Medical Department, United Fruit
Company, New York.



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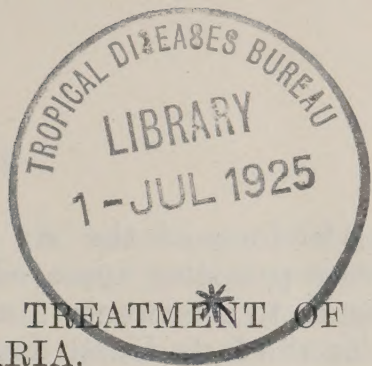
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1925



PREVENTION AND TREATMENT OF MALARIA.

By W. E. DEEKS, M.D.

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Company, New York.*

CLINICAL observations made on patients suffering from general paralysis, dementia præcox, disseminated sclerosis, &c., in whom malarial infection was introduced for therapeutic purposes, have an unusual interest. This method of treatment has been in vogue, in European countries particularly, during recent years, having originated with Wagner-Jauregg in Vienna. A sufficient number of cases have been treated to enable clinical observers to draw fairly accurate conclusions in regard to several hitherto mooted points in the prevention and cure of malaria.

Warrington Yorke and J. W. S. Macfie have reported their observations on 146 cases; and their findings coincide in general with those of other European observers. In their group of treated cases, 105 were inoculated by virulent blood: chiefly subcutaneously—occasionally intravenously. In six cases *Plasmodium malarix* was inoculated, in one case *P. falciparum*, and in ninety-eight cases *P. vivax*. In addition to these, forty-one cases were infected with *P. vivax* through the agency of infected mosquitoes (*Anopheles maculipennis* and *A. bifurcatus*).

These observations made under direct scientific control invite discussion on the following phases of malaria prevention and cure: (1) Immunity; (2) Quinine prophylaxis; (3) Treatment of primary infections; (4) Treatment of chronic infections or relapses.

IMMUNITY.

Some of the observations which refer to the question of immunity may be briefly summarized:

(1) In four of the six cases inoculated with *P. malariae* parasites appeared in the blood from the sixteenth to the twenty-first day after inoculation; in one, on the forty-fourth day; and in one, on the fifty-fourth day.

(2) In those inoculated with *P. vivax* the parasites appeared in the blood in from six to twenty days, and the fever appeared in all cases about the same time, only occasionally preceding or following, by one or two days, the finding of the parasites.

(3) In the ninety-eight cases inoculated with virulent blood nine failed to become infected on the first inoculation. Occasionally repeated inoculations failed to infect. Wagner-Jauregg noted the same in his series of inoculations and met with a few cases which he was unable to infect after three or four inoculations.

(4) Van Loon and Kirschner, of Batavia, report as follows: "A great percentage of the patients, who had lived in the Tropics from their birth, and who were repeatedly (four to five times) intravenously, and afterwards also subcutaneously, inoculated with relatively large quantities of benign tertian blood, appeared to be absolutely immune; others fell ill, but slightly only, and recovered spontaneously after a few attacks."

(5) All of the forty-one cases bitten by mosquitoes became infected. S. P. James, however, reports two cases of failure to infect by this method.

(6) In four of the ninety-eight infected spontaneous cure resulted from five to fourteen days, and no relapses occurred in from three to twelve months' observation.

Immunity to malaria evidently exists in varying degrees in the human subject, as evidenced by the following facts:

(1) That notwithstanding the direct inoculation of 2 c.c. of virulent blood containing approximately a million parasites, nine out of ninety-eight cases failed to become infected and required three to four inocula-

tions to bring about infection. In some cases infection failed after four inoculations, which demonstrates that definite immunity exists in some individuals, particularly among those long resident in tropical malarial districts.

(2) S. P. James has seen two cases whom he was unable to infect by mosquitoes which showed, on subsequent dissection, numerous sporozoites in the salivary glands.

(3) In four of the six cases inoculated with *P. malarix* parasites appeared in the blood from the sixteenth to the twenty-first day after inoculation: in one, on the forty-fourth day; and in one on the fifty-fourth day. Although the same quantity of virulent blood containing quartan parasites was injected in different individuals, the incubation period varied from sixteen to fifty-four days—that is, before parasites appeared in the peripheral blood accompanied by fever.

(4) In four of the ninety-eight cases inoculated with tertian parasites, spontaneous recovery took place in from five to fourteen days. In the remaining cases of this group the incubation period varied from six to twenty days.

Thus in both quartan and tertian infections different degrees of resistance are seen. In other words, it requires more time in some individuals than in others for the development of sufficient parasites to produce symptoms; or, what is much more probable, the agencies concerned in the development of immunity in some individuals is stronger than in others, thus delaying or altogether preventing the onset of symptoms.

If immunity, partial or complete, were non-existent, undoubtedly the population in severely malaria-infected districts would be completely exterminated in a short time.

My experience in Panama confirms the probability of the development of immunity against malaria. Before Panama was sanitated, anopheles were present

in large numbers and new-comers were constantly infected, whereas it was seldom met with in the resident population. From 1906 to 1914 I was frequently called in consultation to see members of the adult resident population, and do not recall a single individual whose illness could be directly attributed to malaria. It was not uncommon, however, to meet with malaria in children or new-comers. Several of the adult residents suffered from organic affections requiring operations, but in most instances these were not followed by malaria exacerbations necessitating the administration of quinine.

Furthermore, I have occasionally met with individuals, past middle life, who said they had never suffered from fever, although they had lived in malaria-infected districts in the tropics for fifteen or more years.

We know that partial immunity is common. An individual may harbour malaria organisms in his blood for years, and yet not be conscious of any discomfort until his general resistance is lowered through some influence, and then a fresh exacerbation of fever ensues.

Yorke and Macfie further demonstrated that immunity, partial or complete, established against one species of the malarial parasite, does not prevent infection from the other species; but it does protect him from fever exacerbations if he is again re-infected with the same parasite by inoculation, or through mosquitoes. Therefore, partial or complete immunity against malaria infection exists or can be developed; but we do not know how, or our problem of prevention and cure would be greatly simplified.

QUININE PROPHYLAXIS.

In regard to the prophylactic use of quinine in preventing infection by mosquitoes, the results from thirty-four cases are shown in the following table:

OBSERVATIONS MADE ON THE EFFECT OF PROPHYLACTIC
QUININE.*From Warrington Yorke and J. W. S. Macfie.*

Number of cases	Prophylactic quinine		Number of infected mosquitoes known to have bitten each case	Result	Incubation period from day of infection	
	Daily dose in grains	Number of days given				
		Before infected mosquitoes fed	The day of, and after, infected mosquitoes fed		Fever	Parasites
5	5	—	7	2-4	All infected	12-17
1	5	1	8	2-4	Infected	20
2	10	5	9	2-4	Both infected	18-20
3	30	—	3	1-3	All infected	11-14
1	30	1	7	1	Not infected	13-14
1	10	—	35	1	Not infected	Observation period six weeks
1	10	—	28	3-4	Not infected	Observation period two months
3	10	—	21	2-4	None infected	Observation period six weeks
6	5	—	56	1-4	None infected	Observation period three months
3	5	7	21	2-5	None infected	Observation period six weeks
2	5	14	14	1	None infected	
1	5	7	14	1	Not infected	
3	5	—	14	2-5	None infected	
1	5	14	10	2	Not infected	
1	5	—	10	1	Not infected	

It is to be noted :

(1) In six cases, 5 gr. of quinine given daily on the day of infection and for about a week subsequently, failed to prevent infection.

(2) In two cases, 10 gr. given five days previous to infection and for nine days subsequently, also failed to prevent infection.

(3) Three cases given 30 gr. daily for three days, beginning with the day of infection, became infected subsequently.

On the other hand

(4) In one case, 30 gr. administered daily, beginning the day previous to, and continuing for seven days subsequent to exposure, prevented infection.

(5) In five cases, 10 gr. daily, administered on the day of infection and for from three to five weeks subsequently, prevented infection.

(6) In seventeen cases, 5 gr. given daily, for from ten to fifty-six days, prevented infection; seven of these cases had taken 5 gr. daily from one to two weeks before infection, the remaining ten beginning with the day of infection.

From these observations we are justified in drawing the following conclusions :

(1) That quinine, given prophylactically in daily doses of from 5 to 30 gr., and for two or three days subsequent to exposure, does not prevent infection; in other words, that quinine has apparently no action whatever upon the sporozoites, and is destructive only to the trophozoites.

(2) That the absence of positive malarial findings in the cases recorded, in observations 4, 5 and 6, as not being infected, does *not* by any means *prove* that the cases were not infected; on the contrary, we are justified in drawing the conclusion that the infection was cured by the subsequent administration of quinine over a period of from ten to fifty-six days.

Dr. H. N. Hanschell records a series of exceedingly

interesting cases which confirm these observations. He had twenty-nine white men under his medical care in Central Africa. Of this number, nine slept under mosquito nets 3 ft. wide. The other twenty slept under mosquito nets 18 in. wide—too narrow for them to avoid exposing their arms and hands to the bites of mosquitoes through the net. All of the twenty-nine men took prophylactic quinine in the form of a 5-gr. tabloid of quinine bisulphate with every evening meal, over a consecutive period of from seventy-eight to 102 days. No infected anopheles were seen about the camps for the greater part of this period. From then on, all those sleeping under 18-in. nets contracted subtertian malaria, the mosquito bites being observed in all instances on the arms and hands which had become exposed when the narrow nets were used. None of the nine men who slept under 3-ft. nets contracted the infection, nor was there any evidence that they had been bitten by mosquitoes. This experience of Dr. Hanschell confirms the observations made by York and Macfie, i.e., that quinine for prophylactic purposes does not prevent infection.

If these conclusions be true, then by the exhibition of quinine for prophylactic purposes we only cloud the issue, and in many cases are unable to determine whether people are infected or not. They may become infected, receive only sufficient quinine to develop a temporary immunity, and remain carriers without symptoms but capable of spreading infection to others. Would it not be a better method of procedure if we permitted them to develop symptoms and thus definitely demonstrate that the organisms are present in the peripheral blood? We could then institute efficient treatment, under proper supervision, and the probabilities are that not only the individual but the community would be benefited more than by our present methods.

It has generally been considered that quinine

destroys not only the sporozoites, but also the malarial organisms when they are free in the plasma, directly after sporulation, and consequently that the best time to administer it, in order to obtain the optimum results, is either about the time of infection or of sporulation, before the liberated organisms have had time to enter the red cells.

The evidence produced above proves almost conclusively that quinine has no effect on the sporozites, and probably not on the organisms in the plasma after sporulation, but only after they have entered the red cells. As stated, this is contrary to the opinion which has been generally accepted.

We have used quinine quite extensively for prophylactic purposes, giving from 15 to 20 gr. twice a week, and have noted that the number of hospital admissions was greatly reduced, and consequently also the rate of serious morbidity. Some recent work in one of the divisions of the United Fruit Company plantations has demonstrated that in those who had been taking 20 gr. twice a week for an extended period of time, infection was present, but that this amount of quinine apparently was sufficient to limit the parasitic development, prevent symptoms, and establish tolerance, as these people did not seek hospital treatment as frequently as they had done previously.

Manson-Bahr claims that there must be at least fifty parasites to the cubic millimetre in order to produce symptoms; and Darling believes that at least twelve gametes to the cubic millimetre are necessary in order to infect mosquitoes. Quinine, in prophylactic doses, may destroy a sufficient number of parasites subsequent to infection to prevent the development of symptoms, although the parasites are still numerous enough to be readily detected in the peripheral blood. In the same manner the gametes could be controlled to such an extent as to prevent mosquito infection. With such results possible, the continuous adminis-

tration of quinine, under certain conditions, is not only justified but commendable.

TREATMENT OF PRIMARY INFECTIONS.

As has been fully demonstrated above, primary infections are readily cured by small daily doses (5 to 1 gr.) given over comparatively short periods (ten to fourteen days) or by larger daily doses (30 gr.) over even shorter periods (seven to ten days). In this connection the following observations were made:

(1) In sixty-one inoculated cases treated by the oral administration of quinine sulphate in solution, 30 gr. daily for three consecutive days, only one relapse occurred during an observation period which varied from four to eighteen months. Wagner-Jauregg, Mühlens and Kirschbaum, Grant and Silverston, and others, report similar results.

(2) In thirteen other cases treated in a similar manner, and subsequently given two or three injections of novarsenobillon, one relapse occurred during a similar observation period.

(3) In the series of forty-one cases infected by mosquitoes, thirty cases were given 30 gr. of quinine daily for three consecutive days, and five relapsed within a period varying from two to six months, the indication being that mosquito infection is more difficult to cure than infection through inoculation, probably because immune bodies were injected with the parasites.

(4) In Hanschell's twenty cases of subtertian malaria, referred to above, the quantity of quinine bisulphate (5 gr. daily) which had been given for a period of from seventy-eight to 102 days, for prophylactic purposes, did not prevent infection. Nevertheless, after the appearance of parasites in the blood it was necessary only to slightly increase the daily dosage for three or four days until a total quantity of 30 gr. had been given orally, and in addition one intramuscular dose of 9 gr., in order to effect a cure.

Most authorities admit, moreover, that the subtertian infections of malaria respond more readily to quinine than quartan and tertian infection.

In this connection, I wish to record the following experience of a friend of mine. Before Port Limon, Costa Rica, was sanitated he resided there for a period of about twenty years. At that time malaria and yellow fever were endemic. In his early experience, he contracted malaria, took very little quinine and developed a chronic intermittent fever, which persisted several weeks after he came North to recuperate. When he recovered his health, he returned to Port Limon and again contracted malaria: he then adopted the following method of treatment:

At the onset of the chill he took a hot foot-bath, drank quantities of hot tea, and covered himself with a number of blankets. To favour free perspiration he retained the heavy covering during the hot and sweating stages. The same night he took two compound cathartic pills, and the next morning (about fifteen to eighteen hours after the onset of the chill) began to take his quinine, 15 gr. in powder (wrapped in tissue paper) every hour, until he had taken 90 gr. Invariably this terminated the attack, and he remained perfectly well for from nine months to two years, that is, until he again became re-infected. He treated most of the men of his camp in the same manner, with invariably excellent results. Undoubtedly these were primary infections, as will be demonstrated later on when the treatment of chronic infections is discussed. It is to be noted that the quinine administration was not begun until the spores had had plenty of time to enter the red-blood cells.

A careful study of the table, as well as these observations, favours the conclusion that in the treatment of primary infections heroic doses (30 to 60 gr. daily) of quinine should be given for the first two or three days, and reduced doses for an additional

week ; or if small doses (5 to 10 gr. daily) are given, the treatment should be continued for from ten to fourteen days or longer, in order to effect a cure. The period of treatment would be largely determined by the physical condition of the patient.

In my early experience in Panama we were accustomed to give 10 gr., three times daily, until the fever disappeared ; and after one or two days of normal temperature the patients were allowed to return to work. It was found that relapses were exceedingly frequent. We then changed our method, and gave 15 gr., three times daily, until the temperature became normal ; and we insisted on our patients remaining in the hospital for at least five days after normal temperature, during which time 10 gr. of quinine were given three times daily, and a very liberal diet ordered. Under this method of treatment the number of relapses was greatly diminished, and the results were so striking that this procedure was officially recognized and adopted as routine treatment. In the light of these recent observations, the occurrence of so few relapses after this method of treatment is adopted can be readily explained by the fact that undoubtedly the majority of these cases were primary infections. We thus have evidence to show that in the treatment of primary infections heroic doses of quinine for the first few days, or smaller doses continued over a period of two weeks, should result in cures in the vast majority of cases.

CHRONIC AND RELAPSING CASES.

In these cases we have a different clinical picture. The patients are anæmic. Not only is the number of red cells reduced below normal, but there is also a loss of hæmoglobin of from 10 to 50 per cent. in the red cells remaining. From this we may infer that either some hæmolytic action is taking place, or else

that the functions of the hæmatopoietic organs are affected. The spleen is enlarged, particularly in the tertian and quartan infections, the function of the liver and kidneys is frequently interfered with, and occasionally these organs are organically diseased. In general, there is a condition of reduced resistance on the part of the patient.

TABLE 2.—SUMMARISING THE RESULT OF VARIOUS SHORT COURSES OF QUININE IN THE TREATMENT OF SIMPLE TERTIAN MALARIA OBTAINED AT LIVERPOOL DURING THE WAR: POST-TREATMENT OBSERVATION PERIOD AT LEAST TWO MONTHS.

From Warrington Yorke and J. W. S. Macfie.

Daily dose in grains and Salt of quinine used	Method of administration	Number of consecutive days quinine given	Number of cases 'treated	Number of relapses	Percentage of relapses
5 sulphate	Oral	2	12	11	91.6
5 hydrochloride	Oral	2	18	18	100
10 sulphate	Oral	2	10	10	100
15 sulphate	Oral	2	14	14	100
15 hydrochloride	Intra- muscular	2	20	19	95
15 alkaloid	Intra- muscular	1-2	38	31	81.6
30 sulphate	Oral	2	14	14	100
45 sulphate	Oral	2	12	9-12	75-100
60 sulphate	Oral	2	12	7	58
90 sulphate, 1st series	Oral	2	76	29	38.1
90 sulphate, 2nd series	Oral	2	89	84-86	94-97
120 sulphate	Oral	2	15	9	60
30 bihydro- chloride	Intra- muscular	12	30	26	86.6

Not infrequently other complicating diseases contribute to the lowering of vitality which is manifestly present. These are the cases which tax the ingenuity of the practitioner if he is to bring about complete convalescence. That we cannot get rid of the malaria infection in many of these cases by the administra-

tion of quinine alone is patent to everyone who has concerned himself with this treatment. The following observations confirm such a statement:—

At Liverpool, during the World War, two-day courses of treatment were given in doses of from 5 to 120 gr. daily; the results, as well as the methods of administration, are shown in Table 2.

Furthermore, twenty-nine cases were given 30 gr. of quinine daily for eight weeks, and 83 per cent. of them relapsed within an observation period of two months.

These were undoubtedly cases of chronic malaria. From these observations we must conclude: First, that brief courses of quinine, no matter how large the dosage, are without value in the treatment of chronic cases; and secondly, that prolonged courses of large doses of quinine, continued over a period of eight weeks, cure only a small percentage of chronic cases. These conclusions are in marked contrast with the results obtained in primary infections—a practical point which should be stressed.

In order to obtain results in this class of cases, in addition to quinine, we must utilize all remedial agents which will tend to increase the natural resistance of the patient as well as combat complicating, debilitating conditions or infections, as apparently quinine alone in any amount over any period of time will not cure some of these chronic relapsing cases.

Among the numerous complicating diseases, in chronic cases resisting quinine, syphilis must be considered. I have repeatedly drawn attention to the fact that this condition must be treated simultaneously with the malaria infection, or our efforts to cure the patient will be futile. It is in this class of cases that the arsenical preparations are of great value, and the good results obtained have often been misinterpreted. Arsenic does not cure the malarial infection, but assists materially in overcoming the debilitating

influences of the complicating syphilis. In the same category as syphilis we may mention hookworm disease, tuberculosis, and all other local or constitutional conditions which tend to lower the resistance of the patient.

Because of the anæmia so generally present, the administration of the arsenical and iron preparations are indicated, and our method of giving two Aiken tonic tablets three times daily over a period of two or three months has proved to be a very useful measure. The formula is :—

Quinine sulphate	...	...	...	1 grain
Reduced iron	...	...	...	$\frac{2}{3}$ "
Strychnine sulphate	...	...	...	$\frac{1}{50}$ "
Arsenious acid	...	...	...	$\frac{1}{50}$ "
Ext. gentian	...	...	...	$\frac{1}{4}$ "

In some of the more stubborn cases every effort to improve the vitality of the patient must be resorted to, and frequently it has been found that a change of climate has proved to be of undoubted value.

It is advisable for us to give consideration to the preparations of quinine which should be used, and the best methods of administration. As to the first—we may administer quinine in the form of the insoluble alkaloid ; or its salts, the sulphate, bisulphate, hydrochloride or bihydrochloride. Some also recommend the tannate, tartrate, or lactate salts, as well as euquinine (an ethyl-ester of quinine-carbonic acid) which are very insoluble preparations, hence almost tasteless, and consequently of value in selected cases. The quinine alkaloid is also practically insoluble. The sulphate is soluble to the extent of one part in 800 parts of water, and the hydrochloride to the extent of one part in thirty-five parts of water. When acid is present in excess these salts enter into solution readily ; the bisulphate one in eighteen parts, and the bihydrochloride in less than its own weight in water.

For hypodermic use, the bihydrochloride salt is to be preferred because of its solubility, but if the

solution has excess acid the injection is very painful. It is better therefore, to use the neutral salt, well diluted, at body temperature, and administer it very slowly.

Sir Leonard Rogers recommends cinchonidine bi-hydrochloride for intramuscular injections.

From observations made recently in our hospitals, the insoluble salts of quinine are as effective therapeutically as the soluble preparations. It is generally believed, however, that quinine in solutions acts more quickly than the insoluble preparations. Solutions must also be used with patients unable to swallow pills, tablets or capsules. Care must always be taken to see that pills and tablets are readily friable, otherwise they will pass through the alimentary tract without absorption.

In the treatment of malignant cases of malaria, quinine must be introduced by the needle; either deep subcutaneously, intramuscularly, or intravenously. The solutions should always be well diluted and introduced very slowly. For intramuscular use, the dilution should be at least one to ten, or twenty. After the injection, the tissues into which the quinine is introduced should be thoroughly massaged, and then a hot-water bottle should be applied, to favour absorption—otherwise tissue necrosis may result. For intravenous use, the dilution with normal saline solution should be still greater, otherwise emboli may result and cause sudden death.

Undoubtedly the intravenous use of quinine is indicated, and is to be selected, when prompt action is necessary in order to save life. Howell claims that it takes about half a minute for a circulating particle of blood to return to any one point, and as the intravenous injection takes longer than this, all infected circulating cells are brought into direct contact with the quinine solution during the period of injection and only those escape which are plugged in the capillaries of the viscera.

It is not definitely known how quinine acts in the cure of malaria, nor what becomes of the major part ingested, but in this connection the following quotation from Cushny is suggestive :

“Quinine appears in the urine within a short time (fifteen minutes) after its exhibition by the mouth. and it continues to be excreted by the kidney in some quantity during the next twenty-hours, and in smaller amounts up to about seventy-two hours. Only about one-third of that absorbed appears in the urine, however, and only traces have been found in the other excretions; so that two-thirds or more undergoes complete destruction in the tissues. When quinine is injected into the subcutaneous tissues some of it is deposited locally and only slowly redissolved, so that traces may be found in the urine for a week or more. When it is injected into the blood it leaves the plasma within a few minutes, becoming attached to the corpuscles in some firm combination from which it is difficult to liberate it. It does not accumulate in any of the organs to any significant extent. It is sometimes stated that a tolerance to quinine may be acquired by prolonged treatment, but this seems to be incorrect, the same symptoms occurring and the same amount appearing in the urine after prolonged administration.”

As based on these observations, the following measures would appear reasonable for the handling of labour camps in malaria-infected districts :

(1) Every effort should be made to obtain a maximum control of mosquito production (not overlooking the economic consideration of costs) by the methods now in general use. These include selection of sanitary camp-sites; and the drainage of pools. Where the latter is not possible, pools should be filled or larvicided by means of petroleum products or Paris green. Seepage areas must be taken care of, and rank vegetation cut as often as necessary.

(2) Dwellings should be screened for those able to

appreciate the value of this measure, and who will care for the screening. Mosquito bars also serve a very useful purpose, if properly constructed—particularly for temporary use. Unless the mosquito net has a width of at least three feet, during sleep the bare arms or legs may come in contact with the net and thus be exposed to mosquito bites. Furthermore, the net should be constructed in the form of an inverted sack and should be securely fastened at the bottom so as to prevent the entrance of mosquitoes. The use of these methods of protection against the biting of mosquitoes applies particularly to the literate and more intelligent members of the community. In order to obtain the maximum results, in conjunction with these measures, these conditions should obtain.

(a) Inhabitants should know that anopheles mosquitoes feed only between sunset and sunrise, and that during this period people should remain behind the screens or bars. Some authorities believe that repellents, such as creosote, offer a satisfactory method of protection.

(b) The people should have more or less definite information in regard to the premonitory symptoms of the malaria infection, which manifest themselves in the form of lassitude, headache, nausea, muscular pains and fever.

(c) They should be familiar, also, with the recognized methods of treatment, the amount of quinine that should be taken daily, and the period over which it should be taken in order to effect a cure.

(d) They should further realize that, if the results of treatment are not satisfactory, skilled medical advice should be sought.

(3) In dealing with the illiterate labourers we are confronted with a more serious problem. They will not appreciate nor take care of the screens or bars, nor observe other precautionary measures. This class of people should have daily or semi-weekly supervision from a trained attendant, who would take their tem-

peratures and obtain brief histories of physical complaints. Those who are suspected of having a malaria infection should be referred to a hospital or sick-camp for daily treatment under direct medical supervision. A trained attendant could supervise in this manner a large number of labourers if they were located in closely adjoining camps with convenient transportation. This method of handling the situation would obviate the necessity of giving large quantities of quinine for prophylactic purposes.

(4) In camps where considerable infection is indicated, a careful survey is strongly recommended, and all those found infected should be treated daily—either in sick-camps or in hospitals. The measures to be adopted would depend upon (a) the degree of infection, and (b) the general physical condition of the patient.

(5) In regard to the chronic relapsing cases: Everything must be done to increase the resistance of the patients by treating complicating diseases or conditions concurrently with the administration of quinine orally or hypodermically, and this necessitates hospitalization under direct medical supervision.

(6) The continuous administration of quinine to all individuals in a camp is justifiable only when there is a high percentage of infection, and when large numbers of infected mosquitoes are present in the neighborhood.

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